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EXAMINER
HUYNH, PHUONG N

ART UNIT	PAPER NUMBER
1644	14

DATE MAILED: 01/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/938,700	MORSEY ET AL.	
	Examiner	Art Unit	
	" Neon" Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *3-6 and 14-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 7-13 and 39-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-41 are pending.

2. Claims 3-6 and 14-38 stand withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

3. In view of the amendment filed 10/30/02, the following rejections remain.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-2, 7-13, and 39-41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) *any* isolated antigenic peptide "**comprising**" an amino acid sequence "consisting of" SEQ IDN O: 4 that induces an anti-IgE immune response that does not cause anaphylaxis when administered to an animal, (2) *any* isolated antigenic fusion protein "**comprising**" an amino acid sequence "consisting of" SEQ ID NO: 4 and a heterologous carrier protein that induces an anti-IgE immune response that does not cause anaphylaxis when administered to an animal, (3) *any* pharmaceutical composition for inducing an anti-IgE immune response that does not cause anaphylaxis comprising *any* one or more antigen peptides consisting of *any* amino acid sequence of amino acid residues of a CH3 domain of *any* IgE molecule or *any* "**fragment thereof**", (4) *any* pharmaceutical composition for inducing an anti-IgE immune response that does not cause anaphylaxis comprising *any* one or more antigen peptides consisting of *any* amino acid sequence of amino acid residues of a CH3 domain of *any* IgE molecule or *any* "**fragment thereof**" wherein at least one antigenic peptide consists of amino acid sequence of SEQ ID NO: 4, (5) *any* pharmaceutical composition for inducing an anti-IgE immune response that does not cause anaphylaxis "comprising" one or more fusion proteins consisting of an amino acid sequence of

amino acid residues of a CH3 domain of *any* IgE molecule or *any* "**fragment thereof**" and *any* heterologous carrier protein, (6) the pharmaceutical composition for inducing an anti-IgE immune response that does not cause anaphylaxis "comprising" one or more fusion proteins consisting of an amino acid sequence of amino acid residues of a CH3 domain of *any* IgE molecule or *any* "fragment thereof" and *any* heterologous carrier protein wherein at least one antigenic fusion protein consists of the amino acid sequence of SEQ ID NO: 4, (7) the pharmaceutical composition for inducing an anti-IgE immune response that does not cause anaphylaxis "comprising" one or more fusion proteins consisting of an amino acid sequence of amino acid residues of a CH3 domain of *any* IgE molecule or *any* "**fragment thereof**" and *any* heterologous carrier protein wherein the heterologous carrier protein is selected from the group consisting of KLH, PhoE, rmLT, TraT and gD from BhV-1 virus, (8) the pharmaceutical compositions mentioned above wherein the anti-IgE immune response is the production of anti-IgE antibodies which bind to soluble IgE in serum and other bodily fluids, prevent IgE from binding to its high affinity receptors on mast cells and basophils, and do not cross-link receptor-bound IgE, (9) the pharmaceutical compositions mentioned above further comprising an adjuvant for preventing IgE from binding to its high affinity receptors on mast cells and basophils and do not cross-link receptor-bound IgE, (10) *any* isolated antigenic peptide "**comprising**" an amino acid consisting of SEQ ID NO: 4 or any "**fragment thereof**", that induces an anti-IgE immune response that does not cause anaphylaxis when administered to an animal, (11) *any* isolated antigenic fusion protein "**comprising**" an amino acid sequence of SEQ ID NO: 4 or *any* "**fragment thereof**" and a heterologous carrier protein that induces of IgE-mediated allergic disorders, that induces an anti-IgE immune response that does not cause anaphylaxis when administered to an animal, and (12) *any* pharmaceutical kit comprising one or more containers filled with one or more antigenic peptides consisting of an amino acid sequence of amino acid residues of a CH3 domain of any IgE molecule or any "fragment thereof" or one or more antigenic fusion proteins consisting of an amino acid sequence of amino acid residues of a CH3 domain of any IgE molecule or any "fragment thereof" and a heterologous carrier protein.

The specification discloses only seven peptides from dog IgE CH3/CH4 domains selected from the group consisting of SEQ ID NO: 1-7 and seven peptides from human IgE CH3/CH4 domains consisting of SEQ ID NO: 8-14 for ascaris desensitization and ameliorating IgE-mediated skin wheal reaction.

With the exception of the specific peptides mentioned above, there is insufficient written description about the structure of any "antigenic peptide" and any "fragment thereof" of CH3 domain of any IgE, much less about function because the term "comprising" is open-ended. It expands the peptide and any "fragment thereof" to include additional amino acid residues at either or both ends. Further, there is insufficient written description about the function of any "fragment thereof" having additional undisclosed amino acids. Given the indefinite number of undisclosed amino acids that can be added to the peptide or fragment thereof, there is insufficient written description about the structure associated with function of any undisclosed peptide or fragment thereof for treating any IgE disorders.

With regard to antigenic fusion protein in claims 2 and 40, there is insufficient written description about the structure associated with function of *any* fusion protein comprising *any* fragment thereof because the term "comprising" is open-ended. It expands the fragment thereof in the fusion protein to include additional amino acid residues at either or both ends. Since the peptide, fragment thereof, fusion protein and fragment thereof are not adequately described, it follows that the pharmaceutical composition comprising said peptide, fragment thereof, fusion protein and fragment thereof is not adequately described. Finally, there are only fourteen peptides (SEQ ID NOS: 1-14) consisting of the CH3-CH4 domains of IgE constant region from only **two species** such as human and dog. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicants' arguments filed 10/30/02 have been fully considered but are not found persuasive.

Applicants' position is that Applicants have amended the claims by limiting the amino acid sequence to "consists of" of SEQ ID NO: 4.

However, the amended claims still recite "comprising" an amino acid sequence "consisting of" SEQ ID NO: 4. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent

protection desired. Further, there is insufficient written description about the "fragment thereof" of SEQ ID NO: 4 because a fragment thereof could be as little as one amino acid. There is also insufficient written description about the fragment thereof "comprising" SEQ ID NO: 4 that has additional undisclosed amino acids, much less having the same function as SEQ ID NO: 4, in turn, would generate anti-IgE specific antibody that could prevent IgE from binding to its high affinity receptors on mast cells and basophils and do not cross-link receptor-bound IgE.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-2, 7-8, 10, 12-13, and 39-41 stand rejected under 35 U.S.C. 102(b) as being anticipated by US Pat No. 5,629,415 (May 1997, PTO 892).

The '415 patent teaches an isolating antigenic peptide such as canine immunoglobulin E protein or fragment thereof which is useful for preparing anti-IgE immune response such as anti-IgE antibody (See reference SEQ ID NO: 2 from amino acid residues 294 to 318, column 7, lines 37-41, in particular). The '415 patent teaches that CH3 and CH4 domains of IgE bind to the Fcε receptor (See column 2, lines 3-4, in particular). The '415 patent teaches canine IgE chimeric proteins (fusion proteins) or conjugate derivatives thereof with or without adjuvant as canine vaccines to treat or prevent IgE mediated-hypersensitivity responses (See column 2, lines 54-61, in particular). The reference pharmaceutical composition such as canine IgE polypeptide or fragment thereof inherently does not cause anaphylaxis when administered to an animal because the reference composition is used as vaccines to treat IgE mediated-hypersensitivity response by inducing the production of anti-IgE antibodies for passive treatment of IgE hypersensitivity where the reference anti-IgE antibodies bind to soluble IgE to prevent IgE from binding to its high affinity receptors on mast cells and basophils and the reference anti-IgE antibodies do not cross-link receptor bound IgE. The reference full-length canine IgE inherently comprises amino acid residues of a CH3 domain of an IgE molecule of the claimed antigenic peptide of SEQ ID NO: 4. The term "comprising" or "has" is open-ended. It expands the claimed antigenic peptide to include additional amino acid residues at either or both ends to read on the reference canine IgE polypeptide. The '415 patent further teaches a pharmaceutical kit comprising the reference IgE

polypeptide or fragment thereof which inherently has an amino acid sequence comprising the residues of a CH3 domain of a canine IgE molecule (See column 9, lines 8-15, in particular). Thus, the reference teachings anticipate the claimed invention.

Applicants' arguments filed 10/30/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) at no point in the '415 patent explicitly disclosed that the canine IgE polypeptide or fragment thereof doe not cause anaphylaxis and (2) Applicants have amended the claims by limiting them to the specific antigen peptide of SEQ ID NO: 4.

However, the claims still recite "comprising" an amino acid sequence "consisting of" SEQ ID NO: 4. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. It is the Examiner's position that the amended claims are not limiting to the specific antigen peptide of SEQ ID NO: 4, especially amended claims 39 and 40. The term "comprising" is open-ended. It expands the peptide to include additional amino acids at either or both ends to include the reference peptides. The reference pharmaceutical composition such as canine IgE polypeptide or fragment thereof inherently does not cause anaphylaxis when administered to an animal because the reference composition is used as vaccines to treat IgE mediated-hypersensitivity response by inducing the production of anti-IgE antibodies for passive treatment of IgE hypersensitivity where the reference anti-IgE antibodies bind to soluble IgE to prevent IgE from binding to its high affinity receptors on mast cells and basophils and the reference anti-IgE antibodies do not cross-link receptor bound IgE.

8. Claims 7, 9 and 12-13 stand rejected under 35 U.S.C. 102(b) as being anticipated by US Pat No. 5,653,980 (Aug 1997, PTO 892).

The '980 patent teaches a vaccine which is a pharmaceutical composition for inducing an anti-IgE antibody immune response that does not cause anaphylaxis comprising one or more antigenic peptides such as CH2-CH3 domains from rat or human having an amino acid sequence comprising amino acid residues of a CH3 domain of an IgE molecule (See entire document, abstract, claims of the '980 patent, in particular). The '980 patent further teaches a pharmaceutical composition comprising one or more fusion proteins such as human or rat CH2-CH3 domains having an amino acid sequence comprising amino acid residues of a CH3 domain

of an IgE molecule fused to a heterologous carrier protein and adjuvant (See column 3, lines 55-65, column 4, lines 51-57, in particular). The reference pharmaceutical composition induces anti-IgE antibodies, which bind to soluble IgE and prevent IgE from binding to its high affinity receptors on mast cells and basophils and do not cause any anaphylactic shock (See column 6, lines 50-52, in particular). The reference composition can be used against all types of IgE-mediated allergies (See abstract, in particular).

Applicants' arguments filed 10/30/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) the '980 patent teaches a fusion of full-length CH2-CH3 domains to a foreign carrier protein and the antibodies induced by the anti-IgE vaccine compositions disclosed in the '980 patent result in anaphylaxis since antibodies against some portions of the CH2 and CH3 domains of the IgE molecule have been shown to cross-link the IgE receptor on the surface of mast cells and basophils and lead to production of mediators of anaphylaxis (Stadler et al). (2) The presently claimed invention induces the production of anti-IgE antibodies, while preventing IgE from binding to its high affinity receptors on mast cells and basophils and preventing cross-linking of receptor-bound IgE.

In response to applicant's argument that the '980 patent result in anaphylaxis since antibodies against some portions of the CH2 and CH3 domains of the IgE molecule have been shown to cross-link the IgE receptor on the surface of mast cells and basophils and lead to production of mediators of anaphylaxis (Stadler et al), the argument of counsel cannot take the place of objective evidence, especially the claims recite an antigenic peptide comprising SEQ ID NO: 4. Since the claimed peptide is open-ended, it expands the claimed peptide to include additional undisclosed amino acid residues at either or both ends to include the reference peptide; hence the fusion protein that would generate anti-IgE immune response, i.e. antibodies to the claimed peptide or fusion protein inherently does not cause anaphylaxis. Further, Applicant has not provided any objective evidence to support the difference between the prior art and instant peptide and fusion protein that would generate antibodies that do not cause anaphylaxis. The record does not contain sufficient objective evidence that the referenced peptide, and fusion protein differ in any significant manner from that claimed.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 9-13 and 41 stand rejected under 35 U.S.C. 103*(a) as being unpatentable over US Pat No. 5,629,415 (May 1997, PTO 892) in view of Harlow et al* in Antibodies a Laboratory Manual, 1988, Cold Spring harbor laboratory publication, Cold Spring Harobr, NY, page 129 (PTO 892).

The teachings of the '415 patent have been discussed supra.

The claimed invention as recited in claim 9 differs from the reference only that the pharmaceutical composition further comprises a heterologous carrier protein.

The claimed invention as recited in claim 10 differs from the reference only that the heterologous carrier protein is selected from the group consisting of KLH.

Harlow *et al* teach protein carrier such as keyhole limpet hemacyanin (KLH) is a useful carrier for coupling non-immunogenic antigen more immunogenic for the production of a strong antibody response (See page 129, in particular).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to fuse the carrier protein such as KLH as taught by Harlow *et al* for a pharmaceutical composition comprising one or more antigenic fusion protein having an amino acid sequence comprising amino acid residues such as a CH3 domain of an IgE molecule or a fragment thereof fused to the carrier proteins such as KLH as taught by the '415 patent and Harlow *et al.* From the combined teachings of the references, it is apparent that one of ordinary

skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because Harlow *et al* teach protein carrier such as keyhole limpet hemacyanin (KLH) is a useful carrier for coupling non-immunogenic antigen to make it more immunogenic for the production of a strong antibody response (See page 129, in particular). The '415 patent teaches an isolating antigenic peptide such as canine immunoglobulin E protein or fragment thereof is useful for preparing anti-IgE immune response such as anti-IgE antibody (See reference SEQ ID NO: 2 from amino acid residues 294 to 318, column 7, lines 37-41, in particular).

Applicants' arguments filed 10/30/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) at no point in the '415 patent explicitly disclosed that the canine IgE polypeptide or fragment thereof doe not cause anaphylaxis and (2) Applicants have amended the claims by limiting them to the specific antigen peptide of SEQ ID NO: 4. (3) The '980 patent teaches a fusion of full-length CH2-CH3 domains to a foreign carrier protein and the antibodies induced by the anti-IgE vaccine compositions disclosed in the '980 patent result in anaphylaxis since antibodies against some portions of the CH2 and CH3 domains of the IgE molecule have been shown to cross-link the IgE receptor on the surface of mast cells and basophils and lead to production of mediators of anaphylaxis (Stadler et al). (2) The presently claimed invention induces the production of anti-IgE antibodies, while preventing IgE from binding to its high affinity receptors on mast cells and basophils and preventing cross-linking of receptor-bound IgE.

However, the amended claims still recite "comprising" an amino acid sequence "consisting of" SEQ ID NO: 4. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. It is the Examiner's position that the amended claims are not limiting to the specific antigen peptide of SEQ ID NO: 4, especially amended claims 39 and 40. The term "comprising" is open-ended. It expands the peptide to include additional amino acids at either or both ends to include the reference peptides. The reference pharmaceutical composition such as canine IgE polypeptide or fragment thereof inherently does not cause anaphylaxis when administered to an animal because the reference composition is used as vaccines to treat IgE

mediated-hypersensitivity response by inducing the production of anti-IgE antibodies for passive treatment of IgE hypersensitivity where the reference anti-IgE antibodies bind to soluble IgE to prevent IgE from binding to its high affinity receptors on mast cells and basophils and the reference anti-IgE antibodies do not cross-link receptor bound IgE.

In response to applicant's argument that the '980 patent result in anaphylaxis since antibodies against some portions of the CH2 and CH3 domains of the IgE molecule have been shown to cross-link the IgE receptor on the surface of mast cells and basophils and lead to production of mediators of anaphylaxis (Stadler et al), the argument of counsel cannot take the place of objective evidence, especially the claims recite an antigenic peptide comprising SEQ ID NO: 4. Since the claimed peptide is open-ended, it expands the claimed peptide to include additional undisclosed amino acid residues at either or both ends to include the reference peptide, hence the fusion protein that would generate anti-IgE immune response, i.e. antibodies to the claimed peptide or fusion protein that inherently does not cause anaphylaxis. Further, Applicant has not provided any objective evidence to support the difference between the prior art and instant peptide and fusion protein that would generate antibodies that do not cause anaphylaxis. The record does not contain sufficient objective evidence that the referenced peptide, and fusion protein differ in any significant manner from that claimed.

12. Claims 9 and 11 stand rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 5,653,980 (Aug 1997, PTO 892) in view of Harlow *et al* in Antibodies a Laboratory Manual, 1988, Cold Spring harbor laboratory publication, Cold Spring Harobr, NY, page 129 (PTO 892).

The teachings of the '980 patent have been discussed supra.

The claimed invention as recited in claim 11 differs from the reference only that the heterologous carrier protein is selected from the group consisting of KLH.

Harlow *et al* teach protein carrier such as keyhole limpet hemacyanin (KLH) is a useful carrier for coupling non-immunogenic antigen more immunogenic for the production of a strong antibody response (See page 129, in particular).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to fuse the carrier protein such as KLH as taught by Harlow *et al* to the amino acid sequence comprising amino acid residues such as the CH2CH3 domains of an IgE molecule as taught by the '980 patent for a pharmaceutical composition comprising one or more antigenic fusion protein having an amino acid sequence comprising amino acid residues such as a

CH2CH3 domains of an IgE molecule or a fragment thereof fused to the carrier proteins such as KLH as taught by Harlow *et al* and the '980 patent. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because Harlow *et al* teach protein carrier such as keyhole limpet hemacyanin (KLH) is a useful carrier for coupling to non-immunogenic antigen to make it more immunogenic for the production of a strong antibody response (See page 129, in particular). The '980 patent teach the reference composition can be used against all types of IgE-mediated allergies and reduces the risk for an allergen mediated release of granule from mast cells and basophilic leukocytes (See abstract, in particular).

Applicants' arguments filed 10/30/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) at no point in the '415 patent explicitly disclosed that the canine IgE polypeptide or fragment thereof doe not cause anaphylaxis and (2) Applicants have amended the claims by limiting them to the specific antigen peptide of SEQ ID NO: 4. (3) The '980 patent teaches a fusion of full-length CH2-CH3 domains to a foreign carrier protein and the antibodies induced by the anti-IgE vaccine compositions disclosed in the '980 patent result in anaphylaxis since antibodies against some portions of the CH2 and CH3 domains of the IgE molecule have been shown to cross-link the IgE receptor on the surface of mast cells and basophils and lead to production of mediators of anaphylaxis (Stadler et al). (2) The presently claimed invention induces the production of anti-IgE antibodies, while preventing IgE from binding to its high affinity receptors on mast cells and basophils and preventing cross-linking of receptor-bound IgE.

However, the amended claims still recite "comprising" an amino acid sequence "consisting of" SEQ ID NO: 4. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. It is the Examiner's position that the amended claims are not limiting to the specific antigen peptide of SEQ ID NO: 4, especially amended claims 39 and 40. The term "comprising" is open-ended. It expands the peptide to include additional amino acids at either or both ends to include the reference peptides. The reference pharmaceutical composition such as

canine IgE polypeptide or fragment thereof inherently does not cause anaphylaxis when administered to an animal because the reference composition is used as vaccines to treat IgE mediated-hypersensitivity response by inducing the production of anti-IgE antibodies for passive treatment of IgE hypersensitivity where the reference anti-IgE antibodies bind to soluble IgE to prevent IgE from binding to its high affinity receptors on mast cells and basophils and the reference anti-IgE antibodies do not cross-link receptor bound IgE.

In response to applicant's argument that the '980 patent result in anaphylaxis since antibodies against some portions of the CH2 and CH3 domains of the IgE molecule have been shown to cross-link the IgE receptor on the surface of mast cells and basophils and lead to production of mediators of anaphylaxis (Stadler et al), the argument of counsel cannot take the place of objective evidence, especially the claims recite an antigenic peptide comprising SEQ ID NO: 4. Since the claimed peptide is open-ended, it expands the claimed peptide to include additional undisclosed amino acid residues at either or both ends to include the reference peptide, hence the fusion protein that would generate anti-IgE immune response, i.e. antibodies to the claimed peptide or fusion protein that inherently does not cause anaphylaxis. Further, Applicant has not provided any objective evidence to support the difference between the prior art and instant peptide and fusion protein that would generate antibodies that do not cause anaphylaxis. The record does not contain sufficient objective evidence that the referenced peptide, and fusion protein differ in any significant manner from that claimed.

13. Claim 41 stands rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 5,653,980 (Aug 1997, PTO 892) in view of US Pat No. 5,629,415 (May 1997, PTO 892).

The teachings of the '980 patent have been discussed supra.

The claimed invention as recited in claim 41 differs from the reference only a pharmaceutical kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions for inducing an anti-IgE immune response that does not cause anaphylaxis comprising one or more antigenic fusion protein having an amino acid sequence comprising amino acid residues of a CH3 domain of an IgE molecule and a heterologous carrier protein.

The '415 patent teaches a pharmaceutical kit such as canine IgE protein in one or more containers (compartmentalized carrier) (See column 8, lines 65-67; column 9, lines 11-13, in particular) filled with one or more ingredients such as labeled antigen or enzyme (See column 9,

lines 15-17, in particular) for screening and measuring the levels of IgE. The '415 patent teaches the kit is useful for detecting the levels of IgE (See column 8, lines 66-67, in particular).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to substitute the canine IgE as taught by the '415 patent for the fusion proteins such as human or rat CH2-CH3 domains having an amino acid sequence comprising amino acid residues of a CH3 domain of an IgE molecule fused to a heterologous carrier protein as taught by the '980 patent for a pharmaceutical kit as taught by the '415 patent and the '980 patent. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the '415 patent teaches the kit is useful for detecting the levels of IgE (See column 8, lines 66-67, in particular). The '980 patent teach the reference composition can be used against all types of IgE-mediated allergies and reduces the risk for an allergen mediated release of granule from mast cells and basophilic leukocytes (See abstract, in particular).

Applicants' arguments filed 10/30/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) at no point in the '415 patent explicitly disclosed that the canine IgE polypeptide or fragment thereof doe not cause anaphylaxis and (2) Applicants have amended the claims by limiting them to the specific antigen peptide of SEQ ID NO: 4. (3) The '980 patent teaches a fusion of full-length CH2-CH3 domains to a foreign carrier protein and the antibodies induced by the anti-IgE vaccine compositions disclosed in the '980 patent result in anaphylaxis since antibodies against some portions of the CH2 and CH3 domains of the IgE molecule have been shown to cross-link the IgE receptor on the surface of mast cells and basophils and lead to production of mediators of anaphylaxis (Stadler et al). (2) The presently claimed invention induces the production of anti-IgE antibodies, while preventing IgE from binding to its high affinity receptors on mast cells and basophils and preventing cross-linking of receptor-bound IgE.

However, the amended claims still recite "comprising" an amino acid sequence "consisting of" SEQ ID NO: 4. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent

protection desired. It is the Examiner's position that the amended claims are not limiting to the specific antigen peptide of SEQ ID NO: 4, especially amended claims 39 and 40. The term "comprising" is open-ended. It expands the peptide to include additional amino acids at either or both ends to include the reference peptides. The reference pharmaceutical composition such as canine IgE polypeptide or fragment thereof inherently does not cause anaphylaxis when administered to an animal because the reference composition is used as vaccines to treat IgE mediated-hypersensitivity response by inducing the production of anti-IgE antibodies for passive treatment of IgE hypersensitivity where the reference anti-IgE antibodies bind to soluble IgE to prevent IgE from binding to its high affinity receptors on mast cells and basophils and the reference anti-IgE antibodies do not cross-link receptor bound IgE.

In response to applicant's argument that the '980 patent result in anaphylaxis since antibodies against some portions of the CH2 and CH3 domains of the IgE molecule have been shown to cross-link the IgE receptor on the surface of mast cells and basophils and lead to production of mediators of anaphylaxis (Stadler et al), the argument of counsel cannot take the place of objective evidence, especially the claims recite an antigenic peptide comprising SEQ ID NO: 4. Since the claimed peptide is open-ended, it expands the claimed peptide to include additional undisclosed amino acid residues at either or both ends to include the reference peptide, hence the fusion protein that would generate anti-IgE immune response, i.e. antibodies to the claimed peptide or fusion protein that inherently does not cause anaphylaxis. Further, Applicant has not provided any objective evidence to support the difference between the prior art and instant peptide and fusion protein that would generate antibodies that do not cause anaphylaxis. The record does not contain sufficient objective evidence that the referenced peptide, and fusion protein differ in any significant manner from that claimed.

14. The following new ground of rejection is necessitated by the amendment filed 10/30/02.

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

16. Claims 1-2 and 39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claims 1-2 and 39 recite the broad recitation "comprising", and the claims also recite "consisting of" which is the narrower statement of the range/limitation.

17. No claim is allowed.

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

20. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
January 13, 2003

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